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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,367	12/09/1998	ULF SCHRODER	REF/SCH29644	1613

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/147,367	SCHRODER, ULF	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *142-193* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *142-193* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 3-22-05 are acknowledged.

Claims included in the prosecution are 142-193.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 142-193 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nasal administration of Diphtheria toxoid or influenza or rota virus antigens in micellar compositions containing monoolein and oleic acid, does not reasonably provide enablement for generic monoglycerides and fatty acid of 6-24 carbon atoms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Instant claims are drawn to generic monoglyceride wherein the fatty acids have 6-24 carbon atom; this virtually includes many fatty acids both saturated and unsaturated; similar is the case with fatty acids with 6-24 carbon atoms. A careful evaluation of the specification indicates that only a combination of monoolein and oleic acids are used and the results obtained as evident from the specification mixed in terms of the claimed effect on specific viruses and bacteria tested compared to art known adjuvant, alum'. Based on these mixed results applicant extrapolates to generic 'antigen' and generic 'administration' and generic

'monoglycerides' and 'fatty acids'. Furthermore, the experiments shown in the specification indicates that the adjuvant is administered together with the bacterial or viral antigen and not separately. Applicant's own experiments indicates unpredictability and therefore, it would require undue experimentation by one of ordinary skill in the art to determine which combinations of monoglycerides and fatty acids would be effective against which virus or bacteria or parasites or cancer antigens. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to specific mode of administration of compositions containing specific monoglyceride and fatty acid for eliciting the immune response to specific organisms.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant traverses the rejection taking into consideration the level of one of ordinary skill in the art to which the inventions pertains and bearing in mind that routine experimentation is permissible for one of ordinary skill in the art to find an enabling disclosure. This argument is not persuasive. As is well known in the art that vaccination against pathogenic viruses such as AIDS virus and influenza virus (to name a few) has proven to be very difficult indicating the unpredictability in the art. Instant claims are drawn in broad terms such as 'antigen', 'monoglycerides' and 'fatty acids'. Based on the unpredictability it would take more than routine experimentation to determine which of the monoglycerides and fatty acids could be used in combination with a specific antigen and still attain the desired function. Furthermore, instant claims are drawn to a method of administration of the adjuvant alone to a host who is already exposed to the antigen.

How can one predict the immune response by the host with the adjuvant alone without undue experimentation? The rejection is maintained.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 142-193 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

One can interpret claims 142 and 143 in two ways. The human or animal is exposed to the antigen such as a virus or bacterium and causing the disease or the normal human or animal is given the antigen for which a vaccine is desired and then administering the claimed composition. It is unclear as to how one can induce immune response in a human or animal having that specific viral or bacterial disease by administering the claimed composition by itself without an antigen. Furthermore, if the animal is already exposed to the antigen, what is the rationale in administering an immunogenic quantity of the antigen and composition again as claimed in claim 151? A careful review of the specification indicates the administration of the antigen and the composition together.

Applicant recites 'consisting essentially of' in claim 142 and therefore, claim 155 which recites the additional ingredients such as surfactants (oleic acid is a surfactant) is inconsistent with claim 142. Similar is the case with claim180, which is dependent from claim 143.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 142-193 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/06921 by itself in combination with Amselem (5,716,637), Wright (5,730,989), Koga (5,352,450), Carrano (5,739,118) individually or in combination.

As pointed out before, WO discloses formulations containing monoglyceride preparation. The preparation contained 98.8% monoglycerides and 1 % free fatty acids. The composition is for the delivery of vaccines (note page 20, lines 25-30, pages 45-47 and claims). What is lacking in WO is the presence of fatty acid in 2 % (instant ratio of monoglyceride to fatty acid is 50:1, claim 92) or in 10 % (claim 93). It would have been obvious to one of ordinary skill in the art to vary the amounts of fatty acid in WO to obtain the best possible results. WO also lacks the teachings of specific pathogen such as influenza or rotavirus recited in instant claims. However, since WO teaches the general applicability of the composition for the delivery of vaccines, it would have been obvious to one of ordinary skill in the art to use the adjuvant taught by WO to any antigen with a reasonable expectation of success.

Amselem teaches oleic acid as one of the components for the delivery of vaccine formulations (note the examples).

Wright while teaching oral vaccine formulations teaches oleic acid as one of the components (note col. 4, lines 11-22).

Koga similarly teaches oleic acid as one of the components in vaccine formulations for preventing dental caries (col. 20, line 59 et seq.).

Carrano teaches oleic acid is a preferred as a genetic vaccine facilitator (col. 14, lines 6-51).

It would have been obvious to one of ordinary skill in the art to add oleic acid in the formulations of WO with the expectation of obtaining at least an additive effect or the best possible results since the references Amselem, Wright, Koga and Carrano each teach that oleic acid is used in vaccine preparations as an adjuvant.

Applicant's lengthy arguments have been fully considered, but are not found to be persuasive. Applicant argues that WO teaches colloidal particles, comprising an interior phase of a non-lamellar reverse cubic, intermediate or hexagonal liquid crystal phase or a homogeneous L3 phase, and a surface phase of a lamellar crystalline or liquid crystalline phase, or an L3 phase and therefore, does not suggest that in present claim. This argument is not found to be persuasive since instant claims do not recite any specific nature of the claimed composition and thus, do not exclude the forms in the prior art. Furthermore, as pointed out in the previous action, the reference teaches the same components, that is, a monoglyceride and a fatty acid and in amounts which are similar to instant amounts and the compositions in both instant invention and WO are

sonicated (see Examples 1-3 on page 8 of instant specification and page 20, line 25 through page 21, line 25; page 31, line 31) and therefore, one would expect the formulations in both to be the same. Applicant's arguments with regard to WO's teachings of fragmenting agent (poloxamer) are not persuasive since a careful review of the specification indicates the use of Pluronic (Example). Furthermore, specification on page 5, line 13 teaches the addition of surfactants (also instant claim 155) and the term, 'surfactants' includes poloxamer since it is a surfactant. Applicant argues that it is known in the art that a monoglyceride preparation, depending upon the purity contains minor amounts of impurities in the form of diglycerides, triglycerides, glycerine and free fatty acids and the amount of impurity fatty acid in the monoglyceride preparation does not exceed 1 % and therefore, in the compositions described in WO there will always be 100 times more monoglyceride than fatty acid. According to applicant, "the adjuvant according to Applicant contains a monoglyceride preparation comprising a minor amount (impurity) of fatty acid, and then an additional amount of free fatty acid together with water while the composition in WO 93/06921 only comprises a monoglyceride with a very small inherent amount (impurity) of free fatty acid. The amount of monoglyceride in Applicant's adjuvant may vary between 0.1 g to 50 g per 100 ml water, while the amount of free fatty acid may vary between 1 to 50 g per 100 mf water. In other words, the adjuvant claimed in the present invention comprises two distinct components and the total amount of free fatty acid exceeds the amount mentioned in WO 93/06921. Moreover, the ratio of monoglyceride to fatty acid does not exceed 50, i.e. there may only be up to 50 times more monoglyceride than fatty acid in the adjuvant composition,

as compared to the ratio of monoglyceride to fatty acid of 100 described in WO 93/06921. These are all claim limitations which cannot be ignored". These arguments are not found to be persuasive since the lower amount of added fatty acid is 1%, which is closer to the amount of 1%, taught by WO and applicant has not shown any unexpected results obtained by increasing the amount of the free fatty acid present in WO's compositions. Furthermore, fatty acids is a broad term and the only example in the specification indicates the use of oleic acid and that too in amounts of 0.5 g per 55 ml of an aqueous medium. The specification contains no data at all on the capability of the composition in enhancing the immune response to an antigen, let alone unexpected results.

Applicant argues that the four publications cited teach oleic acid as one of the components and individually argues against the four references. These arguments are persuasive since the prior art cited is suggestive of the use of oleic acid in ***vaccine formulations*** just as in instant invention and as pointed out above, applicant has not shown any unexpected results by adding this component which prior art already suggests as one of the additives.

Upon consideration, the rejection of claims over the above references in further combination with Isaacs is withdrawn.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK